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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,936	11/17/2000	Y. Tom Tang	21272-096	7761

30623 7590 10/02/2003

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/714,936	TANG ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,11,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1102* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence search results* .

DETAILED ACTION

1. The Preliminary Amendment filed January 4, 2002 has been entered. Claims 1-9, 12-19, and 22-28 have been canceled, and claims 10 and 20 have been amended. Claims 10-11 and 20-21 are now pending and under consideration. It is noted that the paper and computer readable forms of the Sequence Listing filed November 17, 2000 have been entered.

Information Disclosure Statement

2. Regarding the information disclosure statement filed November 4, 2002, it is noted that the examiner has provided a complete citation for document C1.

Specification

3. The title of the invention is not descriptive of the claims under consideration, which are drawn to polypeptides. A new title is required that is clearly indicative of the invention to which the claims are directed.

4. The use of the trademarks GENBANK and UNIGENE has been noted in this application. The trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 10-11 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides encoded by SEQ ID NO: 218 that correspond to fragments of well-known sialyltransferases disclosed in the prior art, does not reasonably provide enablement for the 221 amino acid polypeptide encoded by the open reading frame located at nucleotides 166-828 of instant SEQ ID NO: 218, or for polypeptides corresponding to fragments of that 221 amino acid polypeptide that do not correspond to fragments of well-known, prior art sialyltransferases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

Claims 10-11 are drawn to an "isolated polypeptide encoded by the polynucleotide of SEQ ID NO: 218," with claim 11 being further drawn to a composition

comprising said polypeptide and a carrier. Claims 20-21 are drawn to an "isolated polypeptide encoded by the polynucleotide comprising a nucleic acid sequence which is 99% identical to the nucleic acid sequence of SEQ ID NO: 218," with claim 21 being further drawn to said polypeptide "wherein the polypeptide is provided on a polypeptide array."

It is unpredictable as to whether one of skill in the art could use Applicants' invention in a manner reasonably commensurate with these claims. Regarding the guidance provided in Applicants' specification, it is first noted that the specification discloses that nucleotides 166-828 of instant SEQ ID NO: 218 encode a 221 amino acid polypeptide that is asserted to be 80% identical to a rat alpha 2,6-sialyltransferase (see Sequence Listing entry for SEQ ID NO: 218, as well as Tables 2-4). However, the specification does not provide any evidence (e.g., the results of any assays for sialyltransferase activity) that this particular polypeptide actually functions as a sialyltransferase. Further, the specification does not provide an alignment of this molecule with the prior art sialyltransferase (so as to, e.g., illustrate any homology shared by the molecules in critical functional domains), and does not include any explanation as to why one of skill in the art would be expected to conclude that this 221 amino acid sequence actually possesses the type of sialyltransferase activity exhibited by the molecule with which it shares homology. Absent guidance from the specification, one of skill in the art may look to the teachings of the prior art for further guidance and enablement of a claimed invention. In the instant case, the prior art as exemplified by Sjoberg et al (Journal of Biological Chemistry 217(13):7450-7459 [3/1996]) discloses a

rat alpha 2,6-sialyltransferase (see entire reference, particularly Figure 2); an alignment of Sjoberg et al's molecule with the 221 amino acid sequence encoded by instant SEQ ID NO: 218 reveals that the first 208 amino acids of the rat protein taught by Sjoberg et al are 83% identical to the first 208 amino acids of Applicants' 221 amino acid polypeptide (see sequence search results). However, Sjoberg et al teach that their polypeptide, at 305 amino acids in length, is "the shortest of" 12 cloned sialyltransferases (see page 7453), and further disclose that one of the two protein motifs that characterize sialyltransferases is located at amino acids 215-237 of their polypeptide (see Figure 1). Accordingly, not only is the amino acid sequence taught by Applicants substantially shorter than numerous previously characterized sialyltransferases, but it lacks one of the two motifs that are characteristic of sialyltransferase molecules. Thus, the teachings of the art suggest that the molecule taught by Applicant might constitute, e.g., a portion of a sialyltransferase molecule (e.g., the first two-thirds of a human alpha 2,6-sialyltransferase), a new type of shorter sialyltransferase whose target molecules may or may not be the same as those of an alpha 2,6-sialyltransferase or one of the many other known types of sialyltransferases, or possibly a molecule partially homologous to sialyltransferases but having a different (and uncharacterized) function. The teachings of the specification and of the prior art do not provide sufficient guidance to allow one of skill in the art to conclude how, or even whether, the 221 amino acid sequence taught by Applicants actually functions. While experimentation could clearly be conducted to further characterize the polypeptide taught by Applicants, the outcome of such experiments is completely

unpredictable; it is unknown as to whether Applicants' polypeptide is actually a complete and functional molecule, and, if it is, what the function of the polypeptide may be. Accordingly, the combined teachings of the specification and of the prior art do not enable the use as a sialyltransferase of the 221 amino acid sequence disclosed by Applicant. As it is unpredictable as to whether Applicants' molecule actually has sialyltransferase activity, it would require undue experimentation to employ that molecule as a sialyltransferase.

Applicants' specification further states that the polypeptides of their invention "are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein)" identified in the specification (see page 39), and asserts a variety of possible uses or activities for polypeptides encoded by the numerous nucleotide sequences disclosed in the specification, including "activity related to cytokine, cell proliferation....or cell differentiation" (p. 41), "stem cell growth factor activity" (p. 43), "regulation of hematopoiesis" (p. 45), "bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration" (p. 47), "immune stimulating or immune suppressing activity" (p. 49), "activin- or inhibin-related activities" (p. 55), "chemotactic or chemokinetic activity" (p. 56), "hemostatis or thrombolysis or thrombosis" (p. 57), "cancer cell generation, proliferation or metastasis" (p. 57), "receptor, receptor ligand or inhibitor or agonist of receptor/ligand interactions" (p. 59), and "anti-inflammatory activity" (p. 63). However, the specification does not actually identify which of these asserted utilities corresponds to each of their disclosed molecules, and does not provide evidence that any polypeptide encoded by instant SEQ ID NO: 218 has a specific

function or activity encompassed by one or more of these asserted possible uses. Again, while one of skill in the art could certainly conduct experimentation aimed at determining the actual activity and/or biological function of the 221 amino acid polypeptide encoded by SEQ ID NO: 218, the outcome of such experiments cannot be predicted, and therefore it is unknown and unpredictable as to how this polypeptide might actually be used. The specification also asserts that the polypeptides of their invention can be used "in assays to determine biological activity," in the preparation of antibodies, in assays to quantitate protein levels, to identify tissues, to isolate "correlative receptors or ligands," to screen for inhibitors or agonists, and as "nutritional sources or supplements" (p. 40-41; see also p. 61-63). However, these are general uses applicable to virtually any protein, and none of these general uses constitutes a substantial utility that is in any way specific to a polypeptide encoded by instant SEQ ID NO: 218. It is noted that the enablement requirement of 35 U.S.C. 112, first paragraph requires a teaching of how to carry out a specific, substantial, and credible utility meeting the requirements of 35 U.S.C. 101; accordingly, the disclosure of methods of using polypeptides that are broadly applicable to virtually any polypeptide (e.g., methods of making antibodies, methods of protein detection, etc.) cannot satisfy the "how to use" requirement of 35 U.S.C. 112, first paragraph (see *MPEP* 2164.07).

It is noted that, as discussed further below, Applicants' definition of "polypeptide" is sufficiently broad so as to encompass molecules of "at least about 5 amino acids" that are encoded by SEQ ID NO: 218, and that the teachings of Sjoberg et al and Beattie et al therefore suggest numerous short polypeptides meeting the requirements of the

claims as written (see paragraph 11, below). The fragments suggested by Sjoberg et al and Beattie et al may be used to identify reagents for specific detection of the protein of Sjoberg et al, and as the teachings of the prior art enable the use of such fragments and of Sjoberg et al's polypeptide, these prior art teachings also enable a specific and substantial use for a subset of the numerous fragments encompassed by the instant claims. However, as the specification and the prior art do not enable the use of the 221 amino acid polypeptide disclosed by Applicants, enablement is also lacking for those fragments of this polypeptide that are not identical to fragments suggested by the art. For example, while fragments specific to Applicants' polypeptide could clearly be attached to an array, or used in some manner to prepare antibodies, the use of such arrays or antibodies in detecting or further characterizing a polypeptide whose function is unknown merely constitute further research and experimentation, rather than a specific and substantial use of such fragments. Accordingly, while the combined teachings of the specification and of the art enable polypeptides encoded by SEQ ID NO: 218 that correspond to fragments of well-known sialyltransferases disclosed in the prior art, those teachings do not provide enablement for the 221 amino acid polypeptide encoded by the open reading frame located at nucleotides 166-828 of instant SEQ ID NO: 218, or for polypeptides corresponding to fragments of that 221 amino acid polypeptide that do not correspond to fragments of well-known, prior art sialyltransferases. It would require undue experimentation to use Applicants' invention in a manner reasonably commensurate with the claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20-21 are indefinite over the recitation of the limitation "the polynucleotide comprising a nucleic acid sequence which is 99% identical to the nucleic acid sequence of SEQ ID NO: 218" in claim 20, because there is insufficient antecedent basis for this limitation in the claims.

Claim 21 is indefinite because it is unclear as to whether the claim is drawn to a polypeptide (as suggested by the recitation "The polypeptide of claim 20...") or whether the claim is drawn to an array (as suggested by the recitation "wherein the polypeptide is provided on a polypeptide array"). Further, to the extent that the claim may be drawn to a polypeptide (rather than to an array including that polypeptide), it is unclear as to how the provision of a polypeptide in a particular manner, e.g., on a particular type of substrate, would further limit the polypeptide being claimed. Clarification is required.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 10-11 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sjoberg et al (Journal of Biological Chemistry 271(13):7450-7459 [3/1996]) in view of Beattie et al (European Journal of Biochemistry 239:479-486 [7/1996]).

It is noted that Applicants' specification states that "The terms 'polypeptide' or 'peptide' or 'amino acid sequence' refer to an oligopeptide, peptide, polypeptide or protein sequence or fragment thereof," and further that a "polypeptide 'fragment,' 'portion,' or 'segment' is a stretch of amino acid residues of at least about 5 amino acids" (see page 11). Accordingly, the instant claims are sufficiently broad so as to encompass, e.g., isolated molecules of "at least about 5 amino acids" that are encoded by the recited polynucleotides. It is further noted that the entry in Applicants' sequence listing for SEQ ID NO: 218 illustrates a 221 amino acid sequence encoded by nucleotides 166-828, with a stop codon being located at nucleotides 829-831 (see Sequence Listing entry for SEQ ID NO: 218).

Sjoberg et al disclose a 305 amino acid rat sialyltransferase, ST6GalNAc III (see entire reference, particularly Figure 2). The first 208 amino acids of the sialyltransferase

disclosed by Sjoberg et al are 83% identical to the first 208 amino acids of the 221 amino acid sequence encoded by instant SEQ ID NO: 218, and this 208 amino acid region of homology between the two sequences includes several regions of 5 or more contiguous amino acids that are completely identical (see the sequence alignment provided herewith). Accordingly, the molecule disclosed by Sjoberg et al includes numerous subsequences that are encoded by the polynucleotide of SEQ ID NO: 218 and/or a polynucleotide "comprising a nucleic acid sequence which is 99% identical to the nucleic acid sequence of SEQ ID NO: 218." However, Sjoberg et al teach a full-length, functional protein, and do not disclose any fragments thereof "of at least about 5 amino acids" that are encoded by SEQ ID NO: 218; accordingly, Sjoberg et al do not disclose isolated polypeptides meeting the claims. Beattie et al teach an array of overlapping decapeptides constructed from "the entire sequence of" bovine growth hormone binding protein, and teach the use of such an array in identifying both continuous and discontinuous epitopes located in a protein of interest, and in identifying high affinity antibodies that bind a protein of interest (see entire reference, particularly page 480, left column; page 482, right column; page 485, left column). In view of the teachings of Beattie et al, it would have been *prima facie* obvious to one of ordinary skill in the art to have prepared an array of overlapping decapeptides from the sialyltransferase taught by Sjoberg et al, and thereby to have prepared an array comprising numerous 10 amino acid polypeptides meeting the requirements of the instant claims. An ordinary artisan would have been motivated to have modified the sialyltransferase of Sjoberg et al in this manner in order to have mapped epitopes of the

polypeptide and identified high affinity antibodies useful in identifying the polypeptide, as suggested by Beattie et al. With further regard to claim 11, it is noted that it is a property of such an array that it constitutes a composition comprising polypeptides and a carrier.

Conclusion

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Sequence search results are cited to show the identity shared between the first 208 amino acids of the sialyltransferase of Sjoberg et al and the first 208 amino acids of the amino acid sequence encoded by nucleotides 166-828 of instant SEQ ID NO: 218.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 703/308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana B. Johannsen
September 26, 2003